SUGAR-CONTAINING AMPHIPHILIC OLIGOMERS

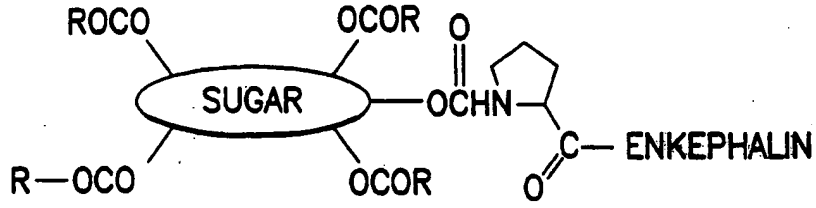


FIG.1A

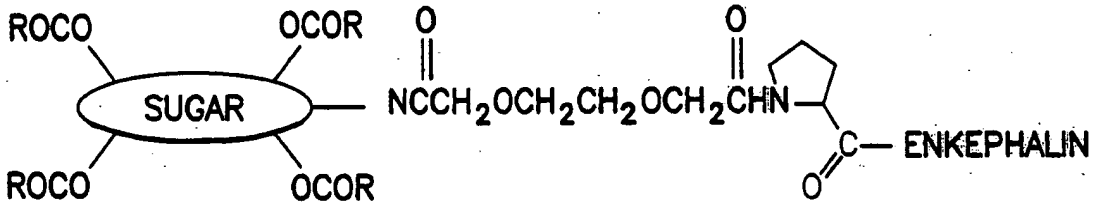


FIG.1B

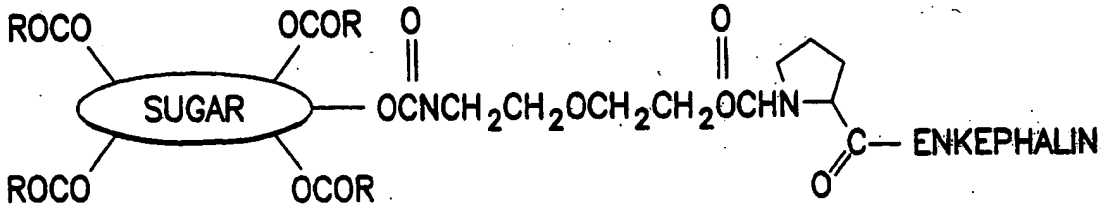


FIG.1C

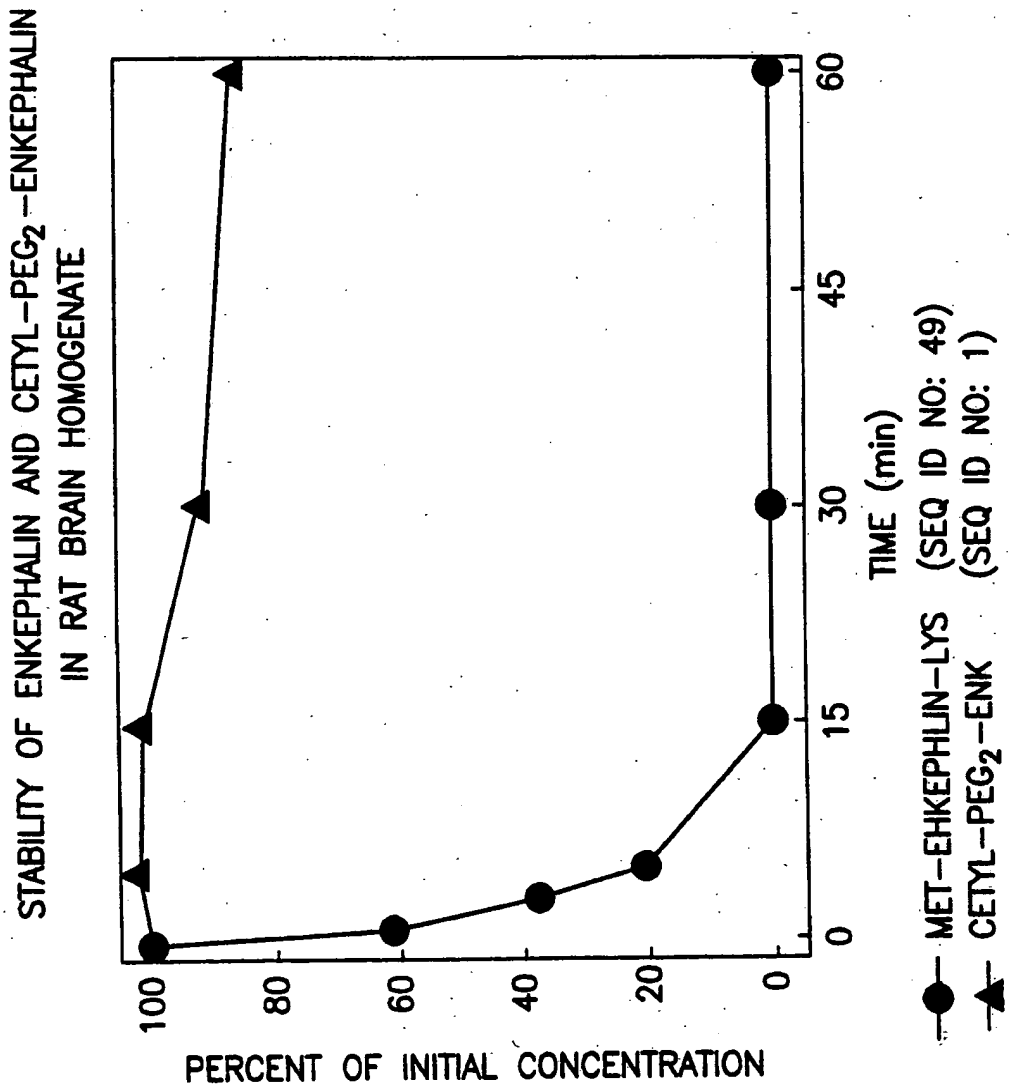

STABILITY OF ENKEPHALIN AND CETYL-PEG2-ENKEPHALIN IN RAT BRAIN HOMOGENATE
PERCENT OF INITIAL CONCENTRATION
100
80
60
40
20
0
0
15
30
45
60
TIME (min)
MET-EHKEPHLIN-LYS (SEQ ID NO: 49)
CETYL-PEG2-ENK (SEQ ID NO: 1)

FIG.2

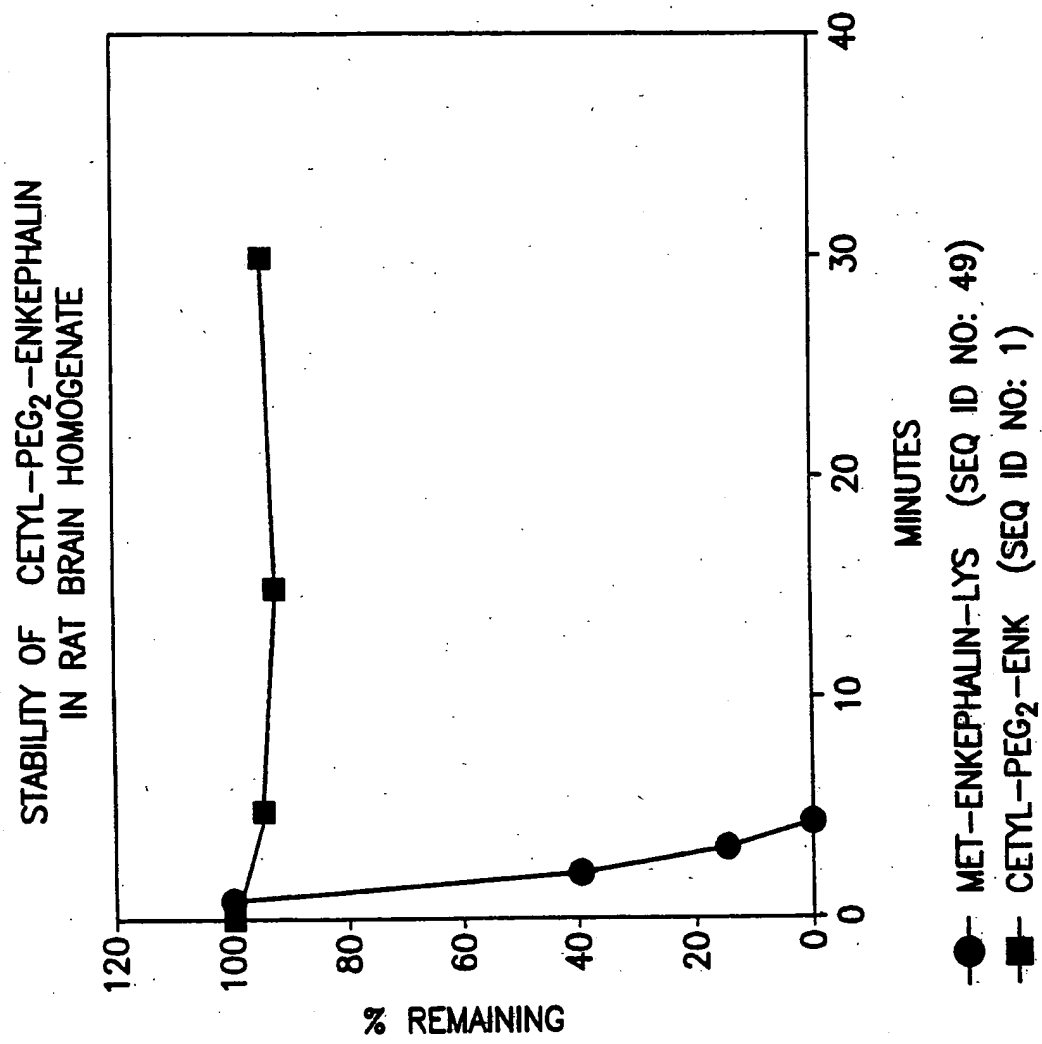

STABILITY OF CETYL-PEG2-ENKEPHALIN
IN RAT BRAIN HOMOGENATE
% REMAINING
120
100
80
60
40
20
0
0
10
20
30
40
MINUTES
MET-ENKEPHALIN-LYS (SEQ ID NO: 49)
CETYL-PEG2-ENK (SEQ ID NO: 1)

FIG.3

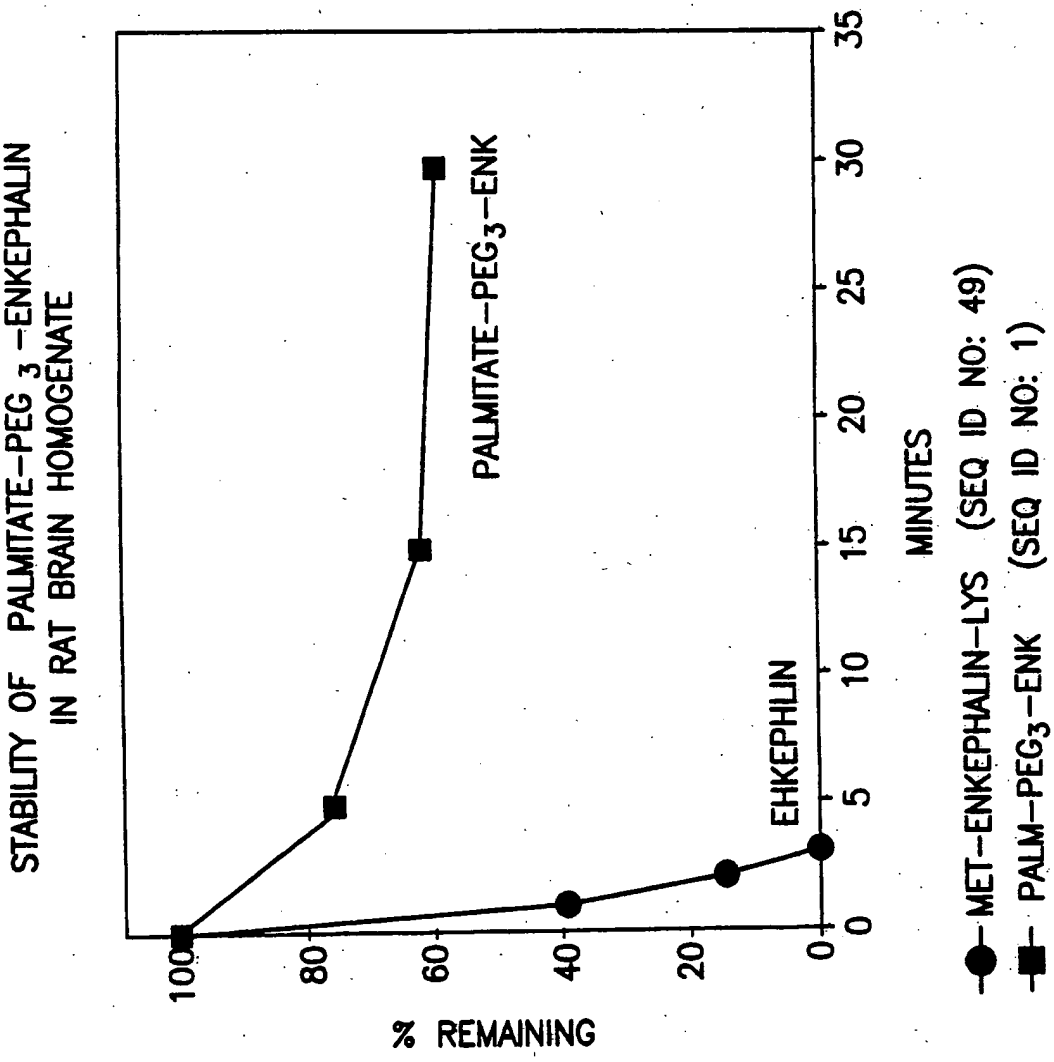

STABILITY OF PALMITATE-PEG 3 -ENKEPHALIN
IN RAT BRAIN HOMOGENATE
% REMAINING
100
80
60
40
20
0
0
5
10
15
20
25
30
35
MINUTES
PALMITATE-PEG3-ENK
EHKEPHLIN
MET-ENKEPHALIN-LYS (SEQ ID NO: 49)
PALM-PEG3-ENK (SEQ ID NO: 1)

FIG.4

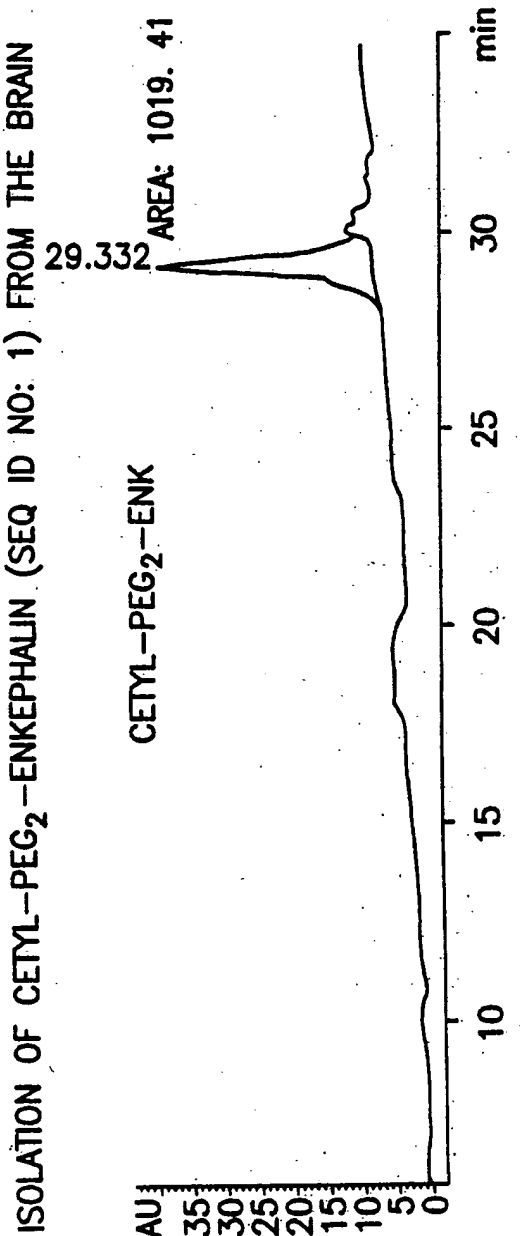

ISOLATION OF CETYL-PEG2-ENKEPHALIN (SEQ ID NO: 1) FROM THE BRAIN
CETYL-PEG2-ENK
29.332
AREA: 1019. 41
mAU
35
30
25
20
15
10
5
0
10
15
20
25
30
min

FIG.5A

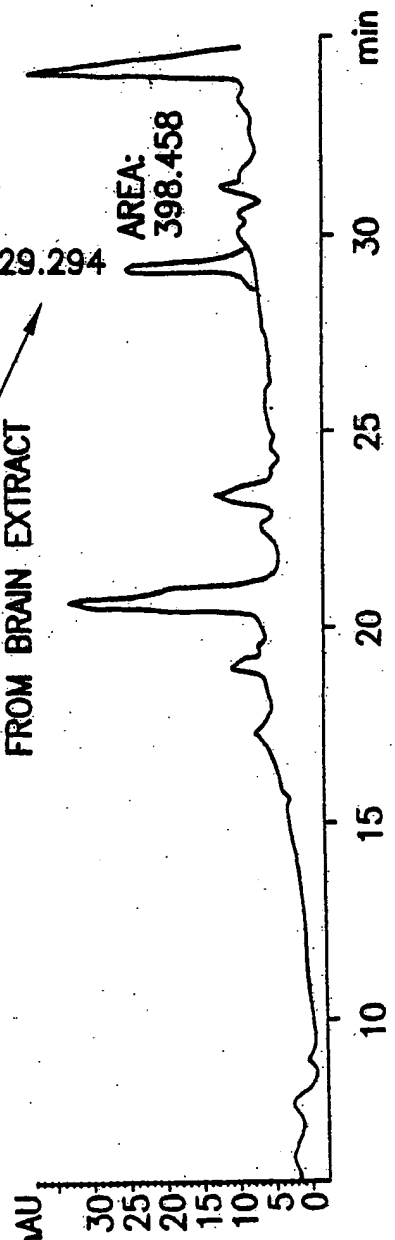

CETYL-PEG2-ENK (SEQ ID NO: 1)
FROM BRAIN EXTRACT
29.294
AREA:
398.458
mAU
30
25
20
15
10
5
0
10
15
20
25
30
min

FIG.5B

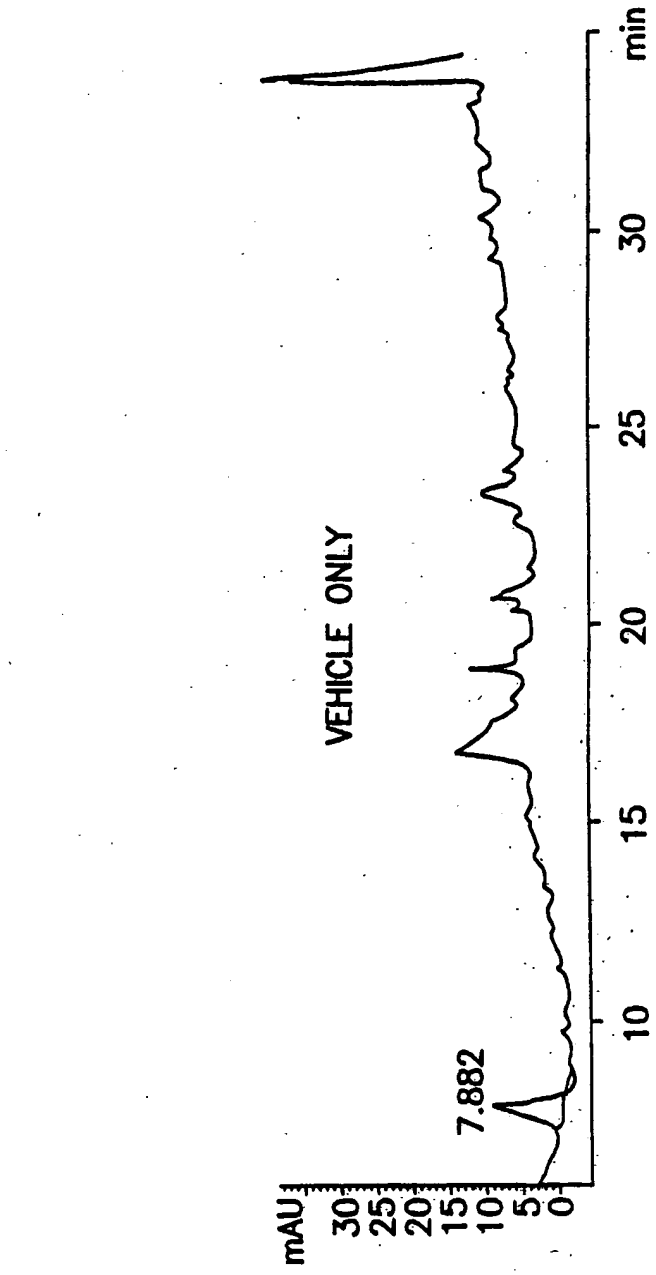

VEHICLE ONLY
7.882
mAU
30
25
20
15
10
5
0
10
15
20
25
30
min

FIG.5C

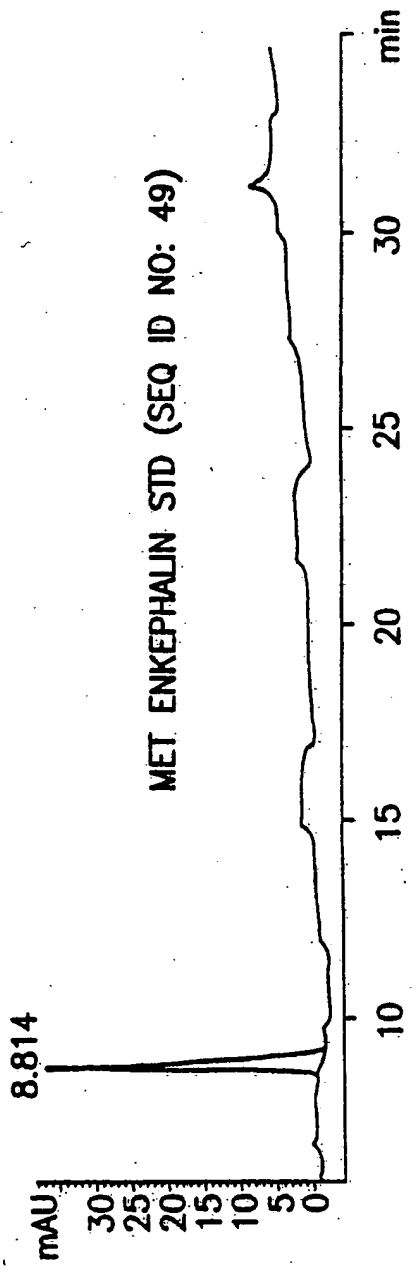

MET ENKEPHALIN STD (SEQ ID NO: 49)
8.814
mAU
30
25
20
15
10
5
0
10
15
20
25
30
min

FIG.5D

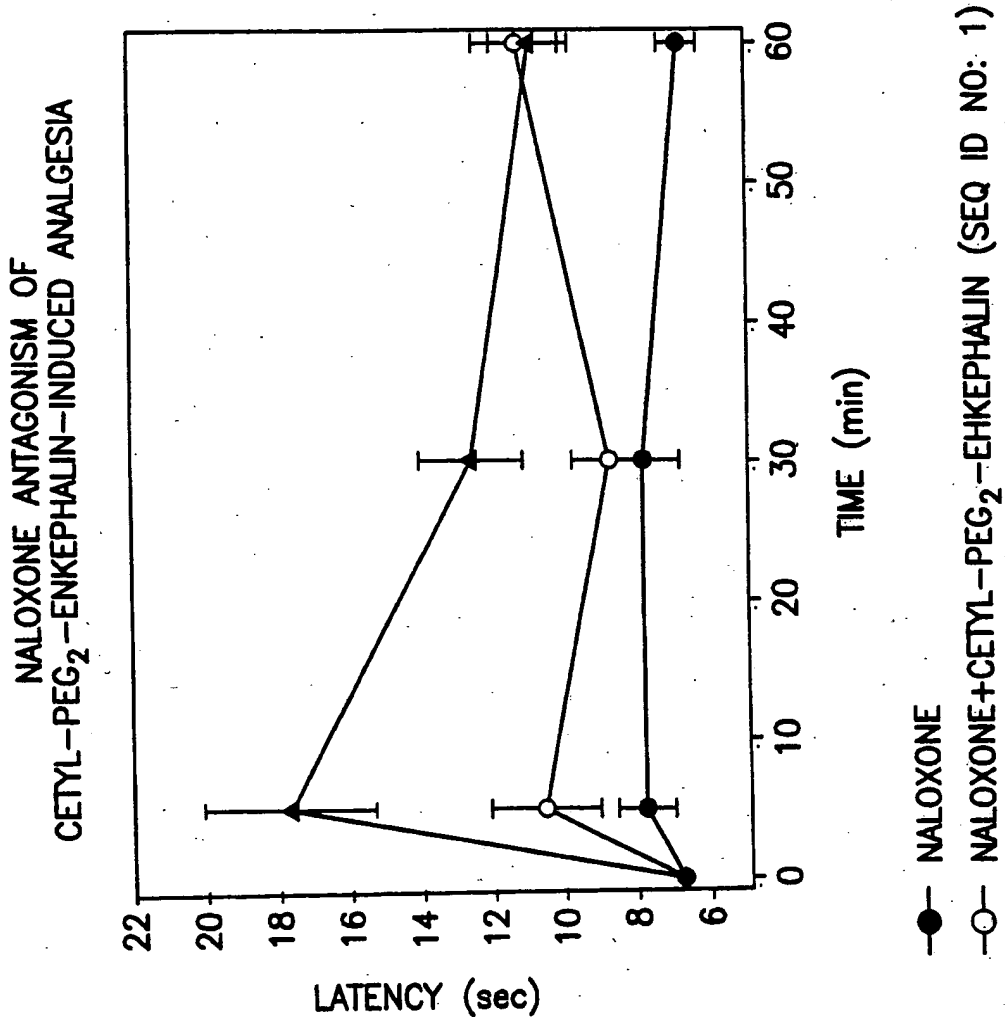

NALOXONE ANTAGONISM OF
CETYL-PEG2-ENKEPHALIN-INDUCED ANALGESIA
LATENCY (sec)
22
20
18
16
14
12
10
8
6
0
10
20
30
40
50
60
TIME (min)
NALOXONE
NALOXONE+CETYL-PEG2-EHKEPHALIN (SEQ ID NO: 1)
CETYL-PEG2-ENKEPHALIN (SEQ ID NO: 1)

FIG.6

ANALGESIC EFFECT OF A 5 mg/kg IV DOSE OF CETYL–PEG_2 –ENKEPHALIN (SEQ ID NO: 1) MONOCONJUGATE IN THE RAT HOT–PLATE ASSAY

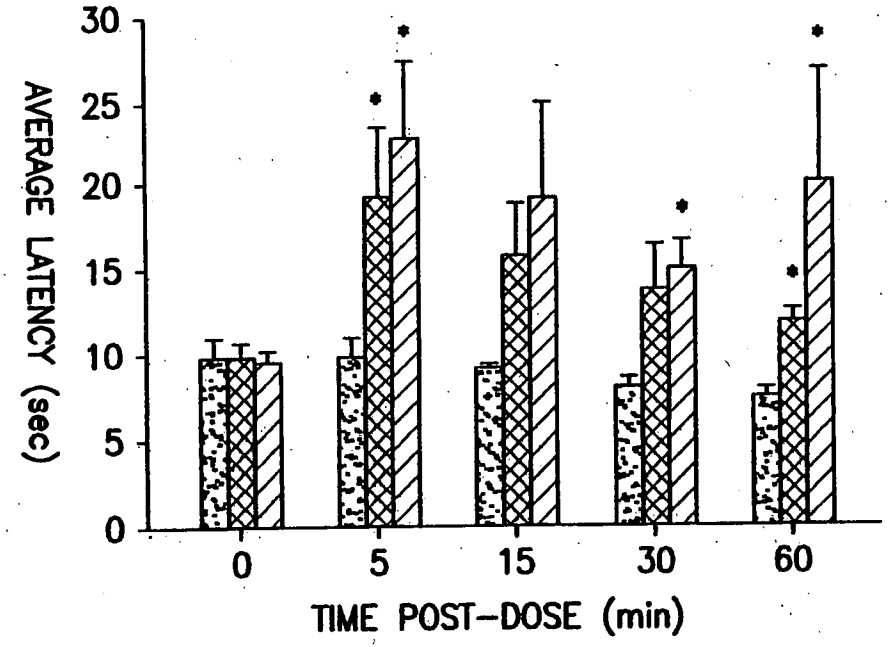
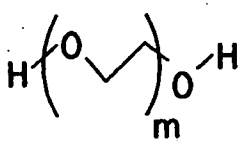


FIG.7

COMPARISON OF μ-RECEPTOR BINDING AFFINITY OF ENKEPHALIN CONJUGATES		
DRUG OR CONJUGATE	DETAILED STRUCTURE	% SPECIFIC BINDING
NALOXONE	NALOXONE	100
ENKEPHALIN	MET-ENKEPHALIN-LYS (SEQ ID NO: 49)	67
CETYL-ENK	CETYL-PEG_2-ENK (SEQ ID NO: 1)	100
CHOL-ENK	CHOLESTEROL-PEG_3-ENK (SEQ ID NO: 1)	95
DHA-ENK	DHA-PEG_2-ENK (SEQ ID NO: 1)	63
PALM-ENK	PALMITATE-PEG_3-ENK (SEQ ID NO: 1)	76
CETYL-TEG-ENK	CETYL-PEG_3-ENK (SEQ ID NO: 1)	100

FIG.8

SYNTHESIS OF OLIGOMER

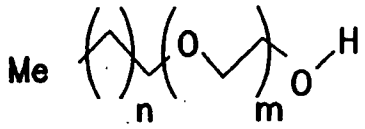


POLYETHYLENE GLYCOL
m=0, 1, 2, 3
(AVERAGE)

BASE

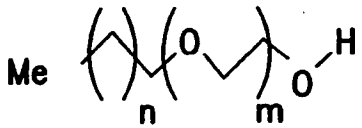
ADDITION

$Me-(CH_2)_nBr$
(BROMO ALKYL DERIVATIVE)
m=15, 17 etc.



AMPHIPHILIC POLYMER

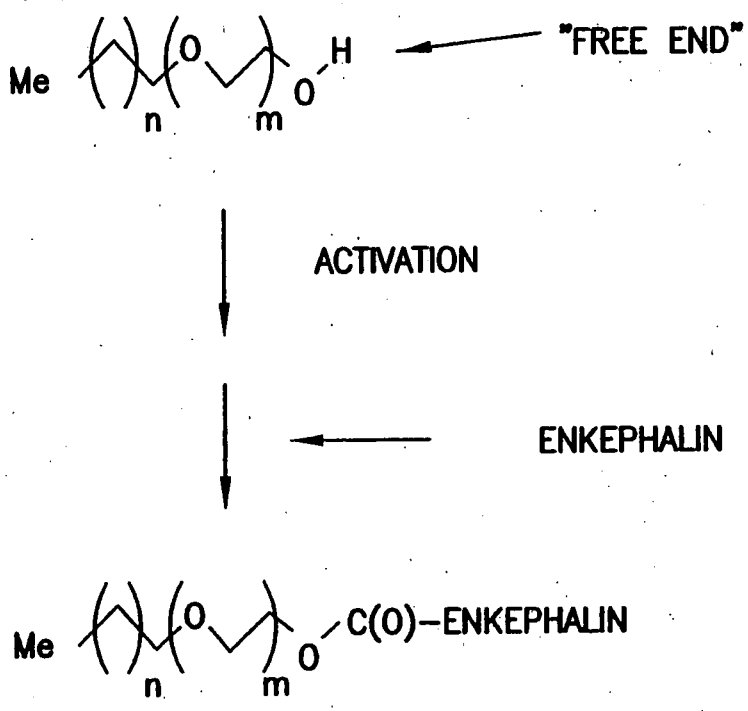
"FREE END"



AMPHIPHILIC POLYMER

FIG.9

ATTACHMENT OF OLIGOMER TO ENKEPHALIN



OLIGOMER–ENKEPHALIN–CONJUGATE

EXAMPLE m=14 AND n=2 CETYL–PEG_2–ENKEPHALIN

FIG.10